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Niagara/Erie County Departments of Health Depew, NY May 23, 2012

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Disclosures



Andrew Kroger is a federal government employee with no financial interest or conflict with the manufacturer of any product named in this presentation

Andrew Kroger will not discuss a vaccine not currently licensed

by the FDA

Disclosures



Andrew Kroger will discuss offlabel uses of meningococcal conjugate vaccine (MCV4) and tetanus toxoid reduceddiphtheria toxoid acellular pertussis (Tdap) vaccine

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What's New in Immunization



Childhood Schedule

Rotavirus Vaccine

Pertussis Vaccine

MCV4 vaccine

Measles Outbreaks

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FIGURE 1: Recommended immunization schedule for persons aged 0 through 6 years—United States, 2012 (for those who fall behind or start late, see the catch-up schedule [Figure 3])

Vaccine ▼ Age ▶	Birth	1 month	2 months	4 months	6 months	9 months	12 months	15 months	18 months	19–23 months	•	4–6 years	
Hepatitis B¹	Нер В	He	рВ				HepB						Range of recommended ages for all
Rotavirus ²			RV	RV	RV^2	•						•	children
Diphtheria, tetanus, pertussis³			DTaP	DTaP	DTaP		see footnote ³	DI	aP		:	DTaP	
Haemophilus influenzae type b⁴		•	Hib	Hib	Hib⁴	h 	Н	ib		•	·		Range of
Pneumococcal⁵			PCV	PCV	PCV		P(CV		•	PF	PSV	recommended ages for certain
Inactivated poliovirus ⁶			IPV	IPV			IPV			• • •	:	IPV	high-risk groups
Influenza ⁷		•		· · · · · · · · · · · · · · · · · · ·	Influenza (Yearly)				////				
Measles, mumps, rubella ⁸							MI	/IR		see footnote®		MMR	
Varicella ⁹					·		Vari	cella		see footnote®		Varicella Varicella	Range of recommended ages for all
Hepatitis A ¹⁰	 	4		 	Dose 1 ¹⁰ HepA Series			children and certain high-					
Meningococcal ¹¹		4		 	MCV4 — see footnote ¹¹				risk groups				

This schedule includes recommendations in effect as of December 23, 2011. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at http://www.cdc.gov/vaccines/pubs/acip-list.htm. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (http://www.vaers.hhs.gov) or by telephone (800-822-7967).

FIGURE 2: Recommended immunization schedule for persons aged 7 through 18 years—United States, 2012 (for those who fall behind or start late, see the schedule below and the catch-up schedule [Figure 3])

Vaccine ▼ Age	► 7–10 years	11–12 years	13–18 years			
Tetanus, diphtheria, pertussis	1 dose (if indicated)	1 dose	1 dose (if indicated)	Range of recommended		
Human papillomavirus ²	see footnote ²	3 doses	Complete 3-dose series	ages for all children		
Meningococcal ³	See footnote ³	Dose 1	Booster at 16 years old			
Influenza ⁴		Influenza (yearly)				
Pneumococcal ⁵	See footnote ⁵					
Hepatitis A ⁶	Complete 2-dose series					
Hepatitis B ⁷	Complete 3-dose series					
Inactivated poliovirus ⁸		Complete 3-dose series				
Measles, mumps, rubella ⁹	Complete 2-dose series					
Varicella ¹⁰	Complete 2-dose series					

This schedule includes recommendations in effect as of December 23, 2011. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at http://www.cdc.gov/vaccines/pubs/acip-list.htm. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (http://www.vaers.hhs.gov) or by telephone (800-822-7967).

FIGURE 3. Catch-up immunization schedule for persons aged 4 months through 18 years who start late or who are more than 1 month behind —United States • 2012

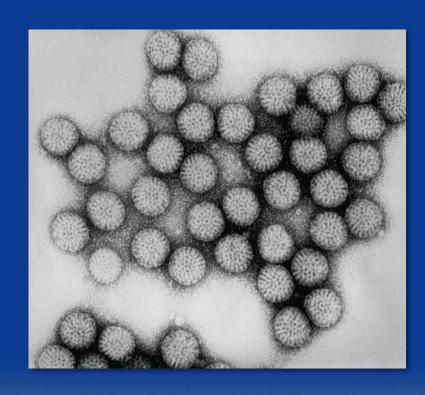
The figure below provides catch-up schedules and minimum intervals between doses for children whose vaccinations have been delayed. A vaccine series does not need to be restarted, regardless of the time that has elapsed between doses. Use the section appropriate for the child's age. Always use this table in conjunction with the accompanying childhood and adolescent immunization schedules (Figures 1 and 2) and their respective footnotes.

Persons aged 4 months through 6 years								
Vaccine Minimum Age for Dose 1		Minimum Interval Between Doses						
		Dose 1 to dose 2	Dose 2 to dose 3	Dose 3 to dose 4	Dose 4 to dose 5			
Hepatitis B	Birth	4 weeks	8 weeks and at least 16 weeks after first dose; minimum age for the final dose is 24 weeks					
Rotavirus¹	6 weeks	4 weeks	4 weeks¹					
Diphtheria, tetanus, pertussis²	6 weeks	4 weeks	4 weeks	6 months	6 months ²			
Haemophilus influerizae type b³	6 weeks	4 weeks if first dose administered at younger than age 12 months 8 weeks (as final dose) if first dose administered at age 12–14 months No further doses needed if first dose administered at age 15 months or older	4 weeks3 if current age is younger than 12 months 8 weeks (as final dose)3 if current age is 12 months or older and first dose administered at younger than age 12 months and second dose administered at younger than 15 months No further doses needed if previous dose administered at age 15 months or older	8 weeks (as final dose) This dose only necessary for children aged 12 months through 59 months who received 3 doses before age 12 months				
Pneumococcal ⁴	6 weeks	4 weeks if first dose administered at younger than age 12 months 8 weeks (as final dose for healthy children) if first dose administered at age 12 months or older or current age 24 through 59 months No further doses needed for healthy children if first dose administered at age 24 months or older	4 weeks if current age is younger than 12 months 8 weeks (as final dose for healthy children) if current age is 12 months or older No further doses needed for healthy children if previous dose administered at age 24 months or older	8 weeks (as final dose) This dose only necessary for children aged 12 months through 59 months who received 3 doses before age 12 months or for children at high risk who received 3 doses at any age				
Inactivated poliovirus⁵	6 weeks	4 weeks	4 weeks	6 months ⁵ minimum age 4 years for final dose				
Meningococcal ⁶	9 months	8 weeks ⁶						
Measles, mumps, rubella ⁷	12 months	4 weeks						
Varicella ⁸	12 months	3 months						
Hepatitis A	12 months	6 months						
	Persons aged 7 through 18 years							
Tetanus, diphtheria/ tetanus, diphtheria, pertussisº	7 years ⁹	4 weeks	4 weeks if first dose administered at younger than age 12 months 6 months if first dose administered at 12 months or older	6 months if first dose administered at younger than age 12 months				
Human papillomavirus¹⁰	9 years		Routine dosing intervals are recommended ¹⁰) (A.S.)				
Hepatitis A	12 months	6 months						
Hepatitis B	Birth	4 weeks	8 weeks (and at least 16 weeks after first dose)					
Inactivated poliovirus⁵	6 weeks	4 weeks	4 weeks ⁵	6 months ⁵				
Meningococcal ⁶	9 months	8 weeks ⁶						
Measles, mumps, rubella ⁷	12 months	4 weeks						
Varicella ⁸	12 months	3 months if person is younger than age 13 years 4 weeks if person is aged 13 years or older						



Rotavirus





Most common cause of severe diarrhea in children

All children worldwide infected by age 5

Improvements in sanitation won't substantially reduce disease incidence

Limited strains in circulation



Rotavirus Disease in the United States



Annually responsible for:

>400,000 physician visits 160,000 emergency dept visits 55,000-70,000 hospitalizations 20-60 deaths

\$300 million in medical costs

\$1 billion in direct and indirect costs





Rotarix – Trials in Latin America and Europe

Any disease 86.6% (86 -87.1)
Severe disease 91.6% (84.7-95.7) RuizPalacios, NEJM 2006, Vesikari T Lancet 2007

RotaTeq - Rotavirus Efficacy and Safety Trial (REST)

Any disease 73.8% Severe disease 98.2%

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Intussusception (IS)



Prolapse of one section of bowel into another section

Most common cause of acute intestinal obstruction in infants younger than 1 year

Can be associated with adenovirus infection and Meckel's diverticulum; cause often unknown

Highest incidence at about 6 months of age (approximately 65 inpatient cases per 100,000 per year)

MMWR 2007;56:218-22





March 19, 1999 / Vol. 48 / No. RR-2

Recommendations and Reports

Rotavirus Vaccine for the Prevention of Rotavirus Gastroenteritis Among Children

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Vol. 48 / No. 43

MMWR November 5, 1999 1007

Withdrawal of Rotavirus Vaccine Recommendation

In July 1999, CDC recommended that health-care providers and parents postpone use of the rhesus rotavirus vaccine-tetravalent (RRV-TV) (RotaShield®*, Wyeth Laboratories, Inc., Marietta, Pennsylvania), for infants, at least until November 1999. This action was based on reports to the Vaccine Adverse Event Reporting System of intussusception (a type of bowel obstruction that occurs when the bowel folds in on itself) among 15 infants who received rotavirus vaccine. Also at that time, the manufacturer, in consultation with the Food and Drug Administration, voluntarily ceased further distribution of the vaccine.

On October 22, 1999, the Advisory Committee on Immunization Practices (ACIP), after a review of scientific data from several sources, concluded that intussusception occurs with significantly increased frequency in the first 1–2 weeks after vaccination with RRV-TV, particularly following the first dose. Therefore, ACIP no longer recommends vaccination of infants in the United States with RRV-TV and withdraws its recommendation that RRV-TV be administered at 2, 4, and 6 months of age. Children who received rotavirus vaccine before July and remain well are not now at increased risk for intussusception.

Rotavirus remains the cause of a substantial health burden for children in the



March 19, 1999 RRV-TV recommended

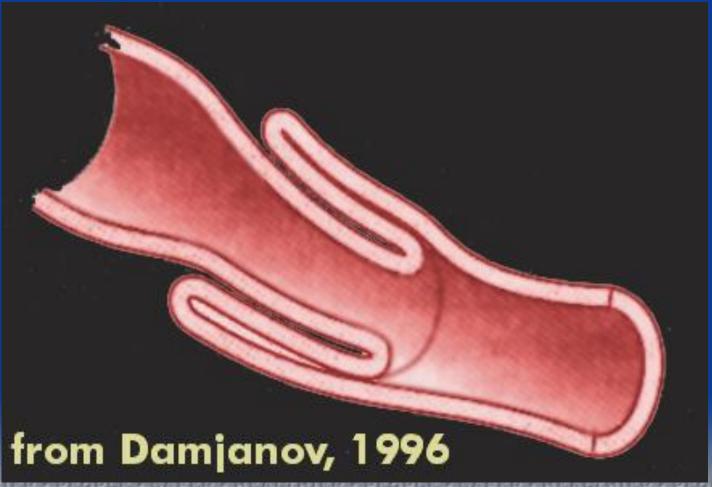
November 5, 1999 RRV-TV recommendation withdrawn

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Intussusception (IS)







Rotavirus Efficacy and Safety Trial (REST)

Phase III trial included 71,799 infants in 11 countries (mostly U.S. and Finland)

No serious adverse reactions identified, including intussusception

New Eng J Med 2006;354:23-33



Rotavirus Vaccine and Intussusception*



	Vaccine Recipients	Placebo Recipients
Within 42 days of vaccination	6 cases	13 cases
Within 1 year of vaccination	13 cases	15 cases

*No increased risk of IS was identified in the Rotarix clinical trials New Eng J Med 2006;354:23-33



Rotavirus Vaccine: Postlicensure Intussusception



Data are mixed as to risk of intussusception following first dose of rotavirus vaccine

Post-licensure trials

World Health Organization (WHO) Cohort study

Mexico, Brazil

Safety surveillance - Australia

CDC case-control studies

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Rotavirus vaccine



Contraindications

Severe Combined Immunodeficiency Disease (SCID)

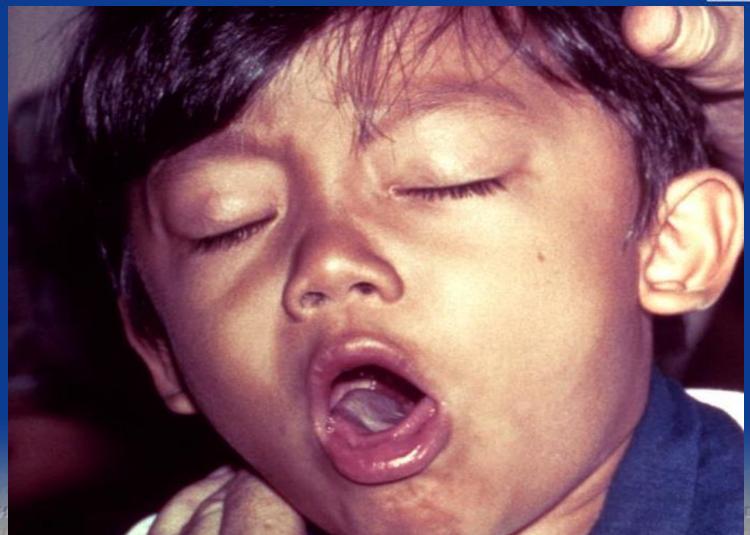
Infants with hx of intussusception
Serious allergy to vaccine component
Rotarix contains latex

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Pertussis









Recent Pertussis Trends

Pertussis cases increased in the late 1990s and early 2000s

2010 - 27,550 pertussis cases

2010 - California - ten infant deaths

Severe illness among young infants with pertussis

Pertussis immunity wanes in 5-10 years

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Source of Infection for Infants With Pertussis

Household contact - 71%

- Parent 55% (mother 37%, father 18%)
- Sibling 16%

Non-household contact - 29%

- Aunt/uncle 10%
- Friend/cousin 10%
- Grandparent 6%

N=44 infants <6 months of age. Pediatr Infect Dis J 2007;26(4):293-9



Tdap Recommendations for Adolescents/Adults



Persons 11 through 64 years of age who have not received Tdap should receive a dose followed by Td booster doses every 10 years

Adolescents should preferably receive Tdap at the 11 to 12 year-old preventive healthcare visit

MMWR 2011; 60 (No. 1):13-5





Children 7 through 18 years of age who are not fully immunized against pertussis (including those never vaccinated or with unknown pertussis vaccination status) should receive a single dose of **Tdap**

off-label recommendation. MMWR 2011; 60 (No. 1):13-5



New Tdap Recommendations for Adolescents



"fully immunized"

- 5 doses of DTaP
- 4 doses of DTaP if 4th administered after the 4th birthday

MMWR 2011; 60 (No. 1):13-5

Adolescent Tdap



Dose of Tdap as 4th, 5th dose of DTaP

Dose of Tdap at 11-12 years

Dose of Tdap given at 7 year – 10 years

Dose of Td (ten years later)

Dose of DTaP at 7 year - 10 years

Provider discretion Dose of Tdap at 11-12
years

н почет топ «Парытногос» « Монирылев Явлети» (вышнихопол » Монкослев Благиу» прав ТМ

Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis (Tdap) Vaccine from the Advisory Committee on Immunization Practices, 2010

Despite sustained high coverage for childhood pertussis vaccination, pertussis remains poorly controlled in the United States. A total of 16,858 pertussis cases and 12 infant deaths were reported in 2009 (1; CDC, unpublished data, 2009). Although 2005 recommendations by the Advisory Committee on Immunization Practices (ACIP) called for vaccination with tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) for adolescents and adults to improve immunity against pertussis, Tdap coverage is 56% among adolescents and <6% among adults (2,3). In October 2010, ACIP recommended expanded use of Tdap. This report provides the updated recommendations, summarizes the safety and effectiveness data considered by ACIP, and provides guidance for implementing the recommendations.

ACIP recommends a single Tdap dose for persons aged 11

the United States, the additional recommendations are made to facilitate use of Tdap to reduce the burden of disease and risk for transmission to infants (Box).

Timing of Tdap Following Td

Safety. When Tdap was licensed in 2005, the safety of administering a booster dose of Tdap at intervals <5 years after Td or pediatric DTP/DTaP had not been studied in adults. However, evaluations in children and adolescents suggested that the safety of intervals as short as 18 months was acceptable (6). Rates of local and systemic reactions after Tdap vaccination in adults were lower than or comparable to rates in adolescents during U.S. prelicensure trials; therefore, the safety of using intervals as short as 2 years between Td and Tdap in adults

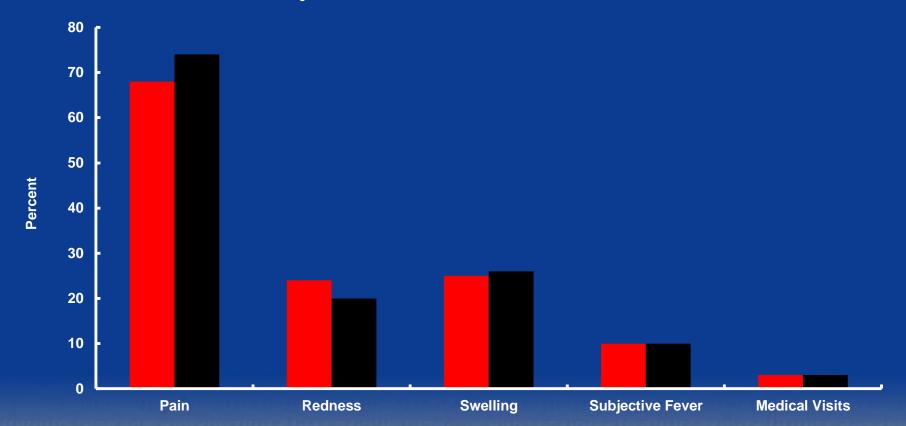
MMWR 2011; 60 (No. 1):13-5



Tdap Adverse Event Rates by Interval Since Previous Td/TT



2 yrs since Td/TT
≥ 2 yrs since Td/TT



Talbot et al. Vaccine 2010;28:3001-7

Solicited Adverse Event



New Tdap Interval Recommendations*



Tdap can be administered regardless of the interval since the last tetanus and diphtheria containing vaccine

ACIP concluded that while longer intervals between Td and Tdap vaccination could decrease the occurrence of local reactions, the benefits of protection against pertussis outweigh the potential risk for adverse events

*off-label recommendation. MMWR 2011; 60 (No. 1):13-5

When to Give Tdap



CDC doesn't recommend a mass recall to give Tdap

If patient in office at high risk of transmitting and acquiring pertussis

- In a pertussis outbreak
- Has or anticipates having contact with infant
- Health-care person

Then disregard interval and give Tdap





Only one recommended dose of Tdap is recommended at this time!

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Violation of Primary Series Intervals



If high risk for pertussis transmission or acquistion give Tdap regardless of interval

Pertussis dose counts, but tetanus and diphtheria will be invalid due to minimum interval violations



Meningococcal Disease







Persons at Highest Risk of Meningococcal Disease or Suboptimal Vaccine Response



Complement deficiency

- High-risk of disease
- Very high antibody titer required to compensate for complement deficiency <u>Asplenia</u>
- High-risk of disease
- evidence of suboptimal response

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Persons with Suboptimal Vaccine Response

HIV infection

evidence of suboptimal response
 Single dose primary series may not be sufficient to confer protection for persons with these high-risk conditions

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MCV4 Primary Series Recommendation



Administer 2 doses of MCV4 at least 8 weeks apart to persons with persistent complement component deficiency and anatomic or functional asplenia

MMWR 2011;60(No. 3):72-6.



MCV4 Primary Series Recommendation



HIV infection is **not** an indication for MCV4

<u>vaccination</u>

However, some persons with HIV infection should receive MCV4 (adolescents, some international travelers, microbiologists, etc)

Persons with HIV infection who are vaccinated with MCV4 should receive 2 doses at least 8 weeks apart

MMWR 2011;60(No. 3):72-6.



FDA Approval: Menactra



June 2011: Menactra (MCV4-D) approved for high-risk infants

2 dose series at 9 months and 12 months

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New MCV4 Recommendations



Certain persons recommended for infant series

Persistent complement component deficiency

Travelers to high-risk meningococcal areas

Infants in a meningococcal outbreak HIV infection (permitted)

New MCV4-D Recommendations



Infant vaccination 2 dose series

Dose 1: 9 months

Dose 2: 12 months

Minimum interval between doses 2 months



Infant Vaccination: Asplenia



Persons with functional or anatomic asplenia NOT recommended for infant vaccination with MCV4-D Still recommended for 2 dose series beginning at age 2 years

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Asplenia



Persons with asplenia are at higher risk for invasive pneumococcal disease

Dose of PCV13 recommended at 12 – 18 months of age

Evidence of interaction between PCV13 and MCV4-D affecting the immune response to PCV13

Because of the risk of interaction, MCV4 not recommended for asplenic children when they should be receiving PCV13









Morbidity and Mortality Weekly Report

Recommendations and Reports

May 27, 2005 / Vol. 54 / No. RR-7

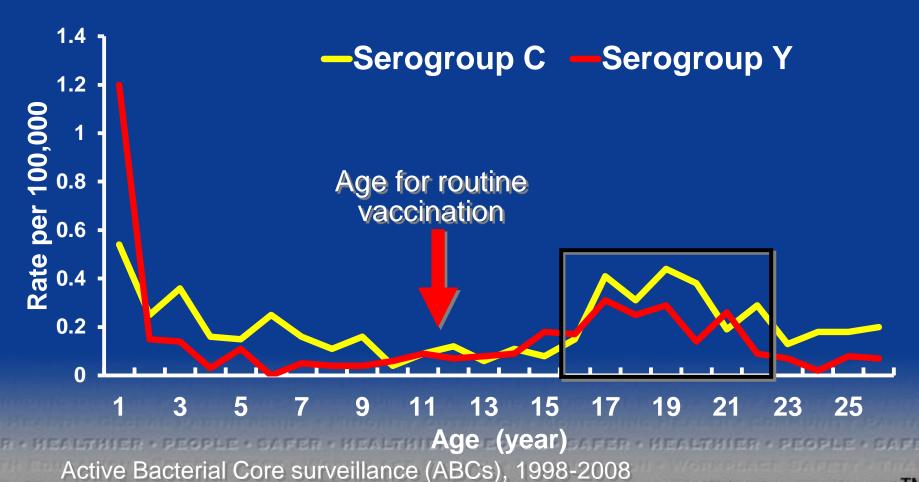
Prevention and Control of Meningococcal Disease

Recommendations of the Advisory Committee on Immunization Practices (ACIP)



Rates of Meningococcal Disease (C and Y) by Age, 1999-2008







Meningococcal Conjugate (MCV4) Routine Revaccination



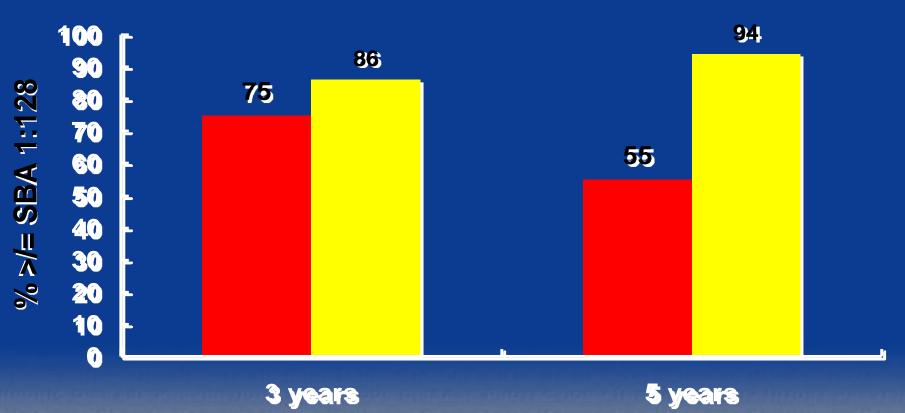
In its 2005 recommendations for MCV, ACIP made no recommendation about revaccination pending the availability of additional data

Serologic data are now available from the manufacturer that show significant decline in antibody 3-5 years after vaccination although few "breakthrough" cases have been reported

MMWR 2009;58(No. 37):1042-3

Seroprotection Rates Following (MCV Vaccination





Years after MCV vaccination

MMWR 2009;58(No. 37):1042-3



Updated Recommendations for Use of Meningococcal Conjugate Vaccines — Advisory Committee on Immunization Practices (ACIP), 2010

On October 27, 2010, the Advisory Committee on Immunization Practices (ACIP) approved updated recommendations for the use of quadrivalent (serogroups A, C, Y, and W-135) meningococcal conjugate vaccines (Menveo, Novartis; and Menactra, Sanofi Pasteur) in adolescents and persons at high risk for meningococcal disease. These recommendations supplement the previous ACIP recommendations for meningococcal vaccination (1,2). The Meningococcal Vaccines Work Group of ACIP reviewed available data on immunogenicity in high-risk groups, bactericidal antibody persistence after immunization, current epidemiology, vaccine effectiveness (VE), and cost-effectiveness of different strategies for vaccination of adolescents. The Work Group then presented policy options for consideration by the full ACIP. This report summarizes two new recommendations approved by ACIP: 1) routine vaccination of adolescents, preferably at age 11 or

Meningococcal disease incidence has decreased since 2000, and incidence for serogroups C and Y, which represent the majority of cases of vaccine-preventable meningococcal disease, are at historic lows. However, the peak in disease among persons aged 18 years (Figure) has persisted, even after routine vaccination was recommended in 2005. In the 2009 National Immunization Survey-Teen, 53.6% of adolescents aged 13 through 17 years had received a dose of meningococcal vaccine (3). From 2000-2004 to 2005-2009, the estimated annual number of cases of serogroups C and Y meningococcal disease decreased 74% among persons aged 11 through 14 years but only 27% among persons aged 15 through 18 years. Cases of meningococcal disease caused by serogroups C and Y among persons who were vaccinated with meningococcal conjugate vaccine have been reported. An early VE analysis that modeled expected cases of disease in vaccinated persons estimated a VE

New MCV4 Recommendations

- administer MCV4 at age 11 or 12 years with a booster dose at 16 years of age
- administer 1 dose at age 13 through 15 years if not previously vaccinated
- for persons vaccinated at age 13
 through 15 years administer a 1-time
 booster dose is recommended,
 preferably at or after 16 through 18
 years of age

*off-label recommendation. *MMWR* 2011;60(No. 3):72-6.



New MCV4 Adolescent Vaccination Recommendations



The minimum interval between doses is 8 weeks

A booster dose is not recommended for healthy persons if the first dose is administered at 16-21 years of age

The booster dose is generally not recommended after the 19th birthday; however, both an initial dose and/or a booster dose can be given to someone between 19 through 21 years old if they are a first-year student living in a residence hall.

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MCV4 vs MPSV4



Conjugate vaccines boost the immune response

If MPSV4 is substituted for MCV4 for the booster dose, or for a primary series dose in high-risk, the dose should be repeated

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MCV Revaccination Recommendations



Other high-risk persons recommended for revaccination

- microbiologists with prolonged exposure to Neisseria meningitidis
- frequent travelers to or persons living in areas with high rates of meningococcal disease

Revaccinate every 5 years as long as the person remains at increased risk

Every 3 years if first dose given between 2 through 6 years of age

- MCV4 for persons 2 through 55 years of age
- MPSV for persons 56 years and older



Measles





In 2011
222 cases of
measles
reported in U.S.
Highest number
since 1996

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MMR



A dose is recommended for travelers between 6 through 12 months of age

Does NOT count toward the two dose routine series

High-risk countries: France, India (generally Europe, Africa, Asia)



MMR



86% percent of cases were not vaccinated or did not know

35% of those eligible had personal or religious belief exemptions

Thank You



Hotline: 800.CDC.INFO

Email: nipinfo@cdc.gov

Website: www.cdc.gov/vaccines

